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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,325	08/10/2001	Martin Gleave	UBC.P-020	8469

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EXAMINER	
VIVLEMORE, TRACY ANN	
ART UNIT	**PAPER NUMBER**
1635	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/913,325	GLEAVE ET AL.	
	Examiner	Art Unit	
	Tracy Vivlemore	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *6,8-17 and 29-34* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6,8,10,12-17,31 and 32* is/are rejected.

7)☒ Claim(s) *9,11,29,30,33 and 34* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Any rejection not reiterated in this Action is withdrawn.

The finality of the last office action and the indicated allowability of claims 8, 10, 12-17, 31 and 32 are withdrawn in view of the following new rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6, 8, 10, 12-17, 31 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bruchovsky et al. (Prostate Suppl. 1996, cited on IDS of 1/9/02) in view of Sensibar et al. (Cancer Research 1995, of record), Kyprianou et al. (Int. J.

Cancer 1997, cited on IDS of 1/9/02) and Raghavan et al. (European Journal of Cancer 1997).

The claimed invention is directed to methods of treating prostate cancer with a combination therapy comprising androgen withdrawal and an antisense oligonucleotide that inhibits expression of TRPM-2. The antisense oligonucleotide can be that designated as SEQ ID NO: 5. In additional embodiments this combination therapy is further combined with a chemotherapeutic agent such as a taxane, an antisense oligonucleotide targeted to another anti-apoptotic protein such as Bcl-2, or both.

Bruchovsky et al. teach that progression of prostate tumors to an androgen independent state can be delayed by maintaining the tumor in a state susceptible to apoptosis. Such maintenance is accomplished by repeated cycles of androgen withdrawal and replacement. Bruchovsky et al. teach that in rats bearing a prostate tumor model such treatment resulted in an increased time period before androgen independence. These experiments demonstrated that cycles of androgen withdrawal and replacement reinduce the apoptotic potential of tumor cells. Similar treatments have been repeated in humans with prostate cancer (see figure 3 and discussion on page 16 under heading "Clinical"). Bruchovsky et al. suggest that intermittent androgen withdrawal therapy can be improved by increasing the number of cycles before androgen independence. Bruchovsky et al. further teach that the different localization of clusterin (another name for TRPM-2) in androgen-dependent and -independent tumor cells indicates deregulation of TRPM-2 expression is promoted by androgen ablation and that TRPM-2 may foster the generation of androgen-independent cells in an androgen depleted environment (see abstract and discussion on page 19 under

heading "Clusterin"). On page 20 Bruchovsky et al. suggest a prostate cancer treatment that includes augmentation of intermittent therapy by administration of additional chemotherapeutic agents such as cytotoxic drugs, radiation or gene therapy. Bruchovsky et al. explicitly suggest anti-TRPM-2 or anti-Bcl-2 gene therapy in conjugation with androgen withdrawal/replacement. Bruchovsky et al. do not teach the use of antisense oligonucleotides as anti-TRPM-2 or anti-Bcl-2 gene therapy.

Sensibar et al. teach phosphorothioate antisense oligonucleotides fully complementary to a nucleic acid encoding Sulfated glycoprotein-2 (an alternative name for TRPM-2), including the translation initiation codon. This sequence is identical to that designated as SEQ ID NO: 5 in the instant application. When transfected into LNCaP cells (a human prostate cancer cell line), these antisense oligonucleotides resulted in a decline of SGP-2 synthesis, indicating that expression of SGP-2 was inhibited (see pages 2433-2435, section entitled "Effect of Antisense Oligonucleotides to SGP-2 on LNCaP Cells"). It is well recognized in the art that antisense inhibition of gene expression is a form of gene therapy.

Kyprianou et al. teach that Bcl-2 expression in prostate tumors is associated with progression to androgen independence. Bcl-2 expression is also correlated with resistance to apoptosis. Kyprianou et al. suggest on page 347 that strategies that inhibit Bcl-2 such as antisense oligonucleotides may enhance prostate cancer treatment.

Raghavan et al. teach that cytotoxic chemotherapeutic agents including mitoxanthrone are commonly used in treatment of prostate cancer. Raghavan et al.

further teach that taxanes such as paclitaxel have promising activity in combination therapies.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to treat prostate cancer with a combination of androgen withdrawal and antisense oligonucleotides directed to TRPM-2, including SEQ ID NO: 5. Bruchovsky et al. provide a motivation to combine androgen withdrawal with TRPM-2 gene therapy; teaching androgen withdrawal is a routine treatment for prostate cancer, showing a link between tumor progression and inappropriate TRPM-2 expression, and explicitly suggesting such combination therapies. One of ordinary skill in the art would have had a reasonable expectation of success in combining androgen withdrawal and antisense oligonucleotide gene therapy because Bruchovsky et al. teach that androgen withdrawal is a routine treatment for prostate cancer and Sensibar et al. teach that antisense oligonucleotides such as that designated as SEQ ID NO: 5 are capable of inhibiting TRPM-2 gene expression.

It would have been further obvious to modify this combination prostate cancer treatment using chemotherapeutic agents and/or antisense oligonucleotides targeted to Bcl-2. Raghavan et al. provide a motivation to use chemotherapeutic agents to treat prostate cancer, teaching that these agents are commonly used and that paclitaxel has shown promise in combination with other treatments. Kyprianou et al. provide a motivation to target Bcl-2 in prostate cancer, teaching a relationship between Bcl-2 expression and progression to androgen independence. Kyprianou et al. and Bruchovsky et al. both suggest that antisense oligonucleotides targeted to Bcl-2 may enhance other prostate cancer therapies. Additionally, Bruchovsky et al. provide a

motivation to use either or both of chemotherapeutic agents and antisense oligonucleotides, suggesting a prostate cancer therapy comprising androgen withdrawal in combination with other therapeutic agents. One of ordinary skill in the art would have had a reasonable expectation of success in combining chemotherapeutic agents or Bcl-2 antisense oligonucleotide therapy with other prostate cancer therapies because Raghavan et al. teach that combination therapies comprising chemotherapeutic agents have been used for treatment of prostate cancer, Kyprianou et al. suggest that combination therapies comprising Bcl-2 inhibition would be useful and suggest use of antisense oligonucleotides to inhibit Bcl-2, and Sensibar et al. demonstrate that antisense oligonucleotides can be used to inhibit expression of a gene associated with prostate cancer.

Thus, the invention of claims 6, 8, 10, 12-17, 31 and 32 would have been obvious, as a whole, at the time of invention.

Allowable Subject Matter

Claims 9, 11, 29, 30, 33 and 34 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see http://pair-direct.uspto.gov.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
March 22, 2006

JAMES SCHULTZ, PH.D.
PRIMARY EXAMINER